

1 **WHAT IS CLAIMED IS:**

2 1. A process for producing a liposome suspension comprising:

3 (a) providing a pre-mixture to an alcohol solvent, wherein the pre-

4 mixture comprises

5 (i) a phospholipid compound comprising 40%-70% of the pre-

6 mixture and selected from the group consisting of lecithin, phosphatidylcholine

7 (PC), phosphatidylethanolamine (PE), phosphatidylglycerol (PG),

8 phosphatidylinositol, sphingomyelin (SM), phosphatidic acids, a di(C₁₂-C₁₈)acyl

9 derivative of any of the foregoing and a combination of any of the foregoing;

10 (ii) a cholesterol comprising 10%-30% (w/w) of the pre-mixture;

11 and

12 (iii) a polyethyleneglycol (PEG)-derived compound comprising

13 15%-30% (w/w) of the pre-mixture and selected from the group consisting of

14 PEG-PE, methoxy- polyethyleneglycol (mPEG)-PE, a di(C₁₂-C₁₈)acyl derivative

15 of either of the foregoing and a combination of any of the foregoing;

16 wherein the ratio of the alcohol solvent to the total amount of

17 compounds (i), (ii) and (iii) is greater than 5:1;

18 (b) mixing the pre-mixture obtained in step (a) with an aqueous

19 ammonium sulfate solution to form a mixture, wherein the ratio of the amount of

20 the pre-mixture obtained in step (a) to the aqueous ammonium sulfate solution is

21 1:2~10 (v/v);

22 (c) subjecting the mixture obtained in step (b) to a pore-extrusion

23 treatment and forming a pre-liposome suspension; and

24 (d) dialyzing the pre-liposome suspension obtained in step (c) with a 5%

1 to 15% sucrose aqueous solution such that a liposome suspension containing
2 liposome particles suspended in the liposome suspension is obtained.

3 2. The process as claimed in claim 1, wherein the alcohol solvent used in
4 step (a) is selected from the group consisting of fatty alcohol, glycol, methanol,
5 ethanol, i-propanol, ethylene glycol, propylene glycol and a combination of any
6 of the foregoing alcohol solvents.

7 3. The process as claimed in claim 1, wherein the alcohol solvent used in
8 step (a) is ethanol.

9 4. The process as claimed in claim 1, wherein the compound (i) used in
10 step (a) is selected from the group consisting of PC, dilauroyl PC, dimyristoyl
11 PC, dipalmitoyl PC, distearoyl phosphatidylcholine (DSPC), dioleoyl PC,
12 dilinoleoyl PC, 1-palmitoyl-2-oleoyl PC and a combination of any of the
13 foregoing compounds.

14 5. The process as claimed in claim 1, wherein the compound (i) used in
15 step (a) is DSPC.

16 6. The process as claimed in claim 1, wherein the compound (iii) used in
17 step (a) is selected from the group consisting of PEG-2000-PE, PEG-3000-PE,
18 PEG-4000-PE, PEG-5000-PE, mPEG-2000-PE, mPEG-3000-PE, mPEG-4000-
19 PE, mPEG-5000-PE, a di(C₁₂-C₁₈)acyl derivative of the foregoing compounds
20 and a combination of any of the foregoing compounds.

21 7. The process as claimed in claim 1, wherein the compound (iii) used in
22 step (a) is selected from the group consisting of PEG-2000-DSPE, PEG-3000-
23 DSPE, PEG-4000-DSPE, PEG-5000-DSPE, 1,2-diacyl-SN-glycero-3-
24 phosphatidyl ethanolamine-N-[methoxy(polyethylene glycol)-2000] and 1,2-

1 diacyl-SN-glycero-3-phosphatidyl ethanolamine-N-[methoxy(polyethylene
2 glycol)-3000], wherein the acyl is myristoyl, palmitoyl, stearoyl or oleoyl.

3 8. The process as claimed in claim 1, wherein the compound (iii) used in
4 step (a) is PEG-2000-DSPE.

5 9. The process as claimed in claim 1, wherein the ratio of the amount of
6 the alcohol solvent to the total amount of compounds (i), (ii) and (iii) is 7~10:1
7 (w/v).

8 10. The process as claimed in claim 1, wherein the compound (i) is
9 DSPC and the compound (iii) is PEG-2000-DSPE in step (a).

10 11. The process as claimed in claim 1, wherein step (a) is carried out at
11 45°C to 70°C.

12 12. The process as claimed in claim 1, wherein step (a) is carried out at
13 55°C to 65°C.

14 13. The process as claimed in claim 1, wherein step (a) is carried out at
15 60°C.

16 14. The process as claimed in claim 1, wherein step (b) is carried out at
17 45°C to 70°C.

18 15. The process as claimed in claim 1, wherein step (b) is carried out at
19 55°C to 65°C.

20 16. The process as claimed in claim 1, wherein step (b) is carried out at
21 60°C.

22 17. The process as claimed in claim 1, wherein the equivalent weight of
23 the aqueous ammonium sulfate solution in step (b) is 0.2N to 0.8N.

24 18. The process as claimed in claim 1, wherein the equivalent weight of

1 the aqueous ammonium sulfate solution in step (b) is 0.4N to 0.6N.

2 19. The process as claimed in claim 1, wherein the ratio of the amount of
3 the pre-mixture obtained in step (a) to the aqueous ammonium sulfate solution is
4 1: 4-8 (v/v).

5 20. The process as claimed in claim 1, wherein the pore-extrusion
6 treatment in step (c) passes the mixture obtained in step (b) through a device
7 having apertures of 0.05 μ m to 0.45 μ m.

8 21. The process as claimed in claim 20, wherein the device is selected
9 from the group consisting of a syringe having apertures, a filter containing a
10 ceramic filtration membrane or a polycarbonate filtration membrane and a plate
11 or tube having apertures.

12 22. The process as claimed in claim 1, wherein the pore-extrusion
13 treatment in step (c) is composed of two steps and first passes the mixture
14 obtained in step (b) through a filter having large apertures and then through a
15 filter having small apertures.

16 23. The process as claimed in claim 22, wherein the large apertures are
17 0.1 μ m and the small apertures are 0.05 μ m.

18 24. The process as claimed in claim 1, wherein step (d) is carried out at
19 room temperature.

20 25. The process as claimed in claim 1, wherein the obtained liposome
21 suspension is further lyophilized.

22 26. A process for producing a liposome-encapsulated drug comprising:
23 mixing a selected drug and a liposome suspension produced by the
24 process as claimed in claim 1 to produce a liposome-encapsulated drug

1 containing the selected drug in the liposome particles suspended in the liposome
2 suspension.

3 27. The process for producing a liposome-encapsulated drug as claimed
4 in claim 26, wherein the selected drug is selected from the group consisting of an
5 anthracycline antibiotic and a camptothecin anti-tumor drug.

6 28. The process for producing a liposome-encapsulated drug as claimed
7 in claim 27, wherein the selected drug is selected from the group consisting of
8 doxorubicin, daunorubicin, irinotecan and vinorelbine.

9 29. The process for producing a liposome-encapsulated drug as claimed
10 in claim 27, wherein the selected drug is doxorubicin.

11 30. The process for producing a liposome-encapsulated drug as claimed
12 in claim 26, wherein the selected drug and the liposome suspension are mixed at
13 45°C to 70°C and then reduced to room temperature such that the selected drug
14 is encapsulated in the liposome particles suspended in the liposome suspension.